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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/518,081 | 03/03/2000 | Leland Shapiro | 7049782001 | 5429 |

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| EXAMINER | |
|---|---|
| MOORE, WILLIAM W | |
| ART UNIT | PAPER NUMBER |
| 1656 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
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| 3 MONTHS | 01/09/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/518,081 | SHAPIRO, LELAND | |
| | Examiner | Art Unit | |
| | William W. Moore | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-10,12-17,23-25 and 30* is/are pending in the application.

4a) Of the above claim(s) *5,6,8,9 and 23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,10,12-17 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

Applicant's amendment in the Response filed 14 September 2006, incorporating the limitation of claim 2 at the close of claim 1's preamble and canceling claim 2, has been entered. Claims 11, 18-22, and 26-29 were cancelled, and claims 1, 3, and 9 amended, in the Response filed 5 April 2005. Claims 5, 6, 8, 9, and 23-25 remain withdrawn form consideration as describing a non-elected invention wherein a claimed method requires a modified peptide inhibitor the nature and structure of which differs substantially from that of the elected polypeptide α1-antitrypsin inhibitor. The amendment to claim 1 made 14 September 2006 allows the elected claims 1, 3, 4, 7, 10, 12-17, and 30, to avoid the prior art rejections made in the communication mailed 5 April 2006.

The claims have been reconsidered in view of the Written Description Guidelines published 5 January 2001, Fed. Reg. 66(4): 1099-1111, which indicate, page 1105, that

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art.

This communication is not made final as such reconsideration necessitates statement of new grounds of rejection herein. Reconsideration of the amendment to claim 1 made on 5 April 2005 also necessitates a new ground of rejection as explained below.

### *Claim Objections*

Claim 1 is objected to because of the following informalities: the conjunction "or" is repeated in the terminal, "wherein", clause of claim 1. Appropriate correction, such as deleting the first occurrence of "or" in this clause, is required.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 4, 7, 10, 12-17, and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 6-11, 15, and 34-36 of copending Application No. 10/427,929. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of inhibiting apoptosis in a subject by administering an α1-antitrypsin inhibitor when the subject suffers from any of arthritis, Alzheimer's disease, autoimmune disease, myocardial infarction, stroke, and ischemia-reperfusion injury of the claims pending herein is also a method of treating an animal suffering from induced inflammation by administering an agent exhibiting "mammalian α1-antitrypsin activity" of the copending claims because arthritis, Alzheimer's disease, autoimmune disease, myocardial infarction, stroke, and ischemia-reperfusion injury are all well-known to induce inflammation and a preferred agent for administration in methods of all of the copending claims is α1-antitrypsin. See, e.g., the copending claim 36.

Claims 1, 3, 4, 7, 10, 12-17, and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25, 28, and 29 of copending Application No. 10/669,251. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of inhibiting apoptosis in a subject by administering an α1-antitrypsin inhibitor when the subject suffers from ischemia-reperfusion injury of the claims pending herein is also a method of treating ischemia-reperfusion injury by administering an α1-antitrypsin inhibitor of the copending claims.

These are both provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 7, 10, 12-17, and 30 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the practice of methods of claims 1, 3, 4, 7, 10, 12-17, and 30 wherein a serine protease inhibitor inhibits serine proteases generally, metalloproteases, or other polypeptides in inhibiting apoptosis, apart from the inhibition of the proteolytic activity of a caspase, a granzyme, or a cathepsin. Instead, the specification discloses at pages 2 and 3 that the role of serine protease inhibitors, such as the inhibitor TLCK, in apoptosis is more likely mediated by inhibiting cysteine proteases. The specification proposes no proteases other than caspases, granzymes, and cathepsins that may be affected by a serine protease inhibitor, including the elected α1-antitrypsin inhibitor, in the remaining seventeen pages of its disclosure. Neither the claims nor the specification describe any protease other than caspases, granzymes, and cathepsins that mediates apoptosis and is inhibited by a serine protease inhibitor and the specification also fails to disclose that an α1-antitrypsin inhibitor is delivered to the cytosolic or nuclear compartments of any mammalian cell that may undergo apoptosis in tissues wherein the medical conditions recited in claim 1 transpire, e.g., neurons, epithelial cells, muscle cells, or connective tissue cells. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description

requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of proteases or other polypeptides that may be the target of a serine protease inhibitor amenable to an inhibition of apoptosis mediated by proteolytic activity in a cell. The specification's treatment of the generic inhibition contemplated by the elected claims is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict that any proteases other than caspases, granzymes, and cathepsins might be inhibited in order to inhibit apoptosis in the medical conditions recited in claim 1.

Claims 1, 3, 4, 7, 10, 12-17, and 30, are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for a method of inhibiting apoptosis mediated by the proteases disclosed in the specification to initiate apoptosis, i.e., caspases, granzymes, and cathepsins, using a serine protease inhibitor to which the cells in tissues affected by the medical conditions recited in claim 1 are impermeable. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice a method of the invention commensurate in scope with these claims.

Claims 1, 3, 4, 7, 10, 12-17, and 30 contemplate the inhibition of apoptosis in a subject by the elected protease inhibitor which is a polypeptide that is primarily diffused throughout the plasma of the circulatory system. The specification does not teach, and the prior art of record herein does not disclose, how to introduce an α1-antitrypsin inhibitor within the cytosolic and nuclear compartments of nervous, muscular, epithelial, or connective tissue cells, i.e., the particular cellular compartments wherein caspases, granzymes, and cathepsins are known to mediate the process of apoptosis. Indeed, if the cells of such tissues were permeable to α1-antitrypsin inhibitor in their native state, including nucleated cells in the blood which are considered to be connective tissue cells, the inhibitor would be delivered to at least the cytosolic compartment of such cells by diffusion from the circulatory system. The specification nowhere suggests how to deliver α1-antitrypsin inhibitor to cytosolic or nuclear compartments of cells of nervous,

muscular, epithelial, or connective tissues in order that it might interact with caspases, granzymes, or cathepsins, and the prior art of record also lacks such a suggestion. It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing eight factors relevant to analysis of enablement). Applying the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for introducing the α1-antitrypsin inhibitor into the cytosolic or nuclear compartments of mammalian cells to interact with the proteases disclosed to mediate apoptosis,

b) the specification lacks working examples wherein the α1-antitrypsin inhibitor is introduced into the cytosolic or nuclear compartments of mammalian cells in order to interact with the proteases disclosed to mediate apoptosis,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support introduction of the α1-antitrypsin inhibitor into the cytosolic or nuclear compartments of mammalian cells, and,

d) unpredictability exists in the art where no other polypeptide protease inhibitor has been introduced into the cytosolic or nuclear compartments of mammalian cells so that it might inhibit activities of a caspase, a granzyme, or a cathepsin.

Thus the scope of subject matters embraced by the claimed methods to be practiced with the elected subject matter is unsupported, on the present record, by the teachings of the specification even if taken in combination with teachings available in the prior art.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 7, 10, 12-17, and 30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendment to claim 1 of 14 September 2006 is indefinite where the recitation "at least one of Alzheimer's disease . . . Downs Syndrome . . . or neurodegenerative

disease" combines terms describing specific neurodegenerative medical conditions, "Alzheimer's disease" and "Downs Syndrome", with a new term, "neurodegenerative disease", that describes multiple medical conditions. The artisan and the public seeking to ascertain the metes and bounds of the intended subject matter cannot determine whether a "neurodegenerative disease" to be treated by administering an elected serine protease inhibitor includes or excludes conditions other than "Downs Syndrome" and "Alzheimer's disease". Claims 3, 4, 7, 10, 12-17, and 30 are included in this rejection because they fail to clarify the metes and bounds of claim 1 from which they depend. Amending claim 1 either to delete the term "neurodegenerative disease" from claim 1 or to remove the terms "Alzheimer's disease" and "Downs Syndrome" from the claim in favor of introducing them in a separate dependent claim will overcome this rejection.

*Conclusion*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
27 December 2006

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER